## REMARKS

Claims 69-81 are pending. Claims 69, 70, 72, 74-81 are rejected.[1] Claims 71 and 73 are not rejected, but have not been indicated as allowable. Claim 75 is objected to.

The outstanding rejections under section 112, first paragraph (enablement); section 112, first paragraph (written description); section 112, second paragraph (indefiniteness); section 102; and Section 103 are withdrawn.

Claims 70, 72, 74, 80 and 81 are newly rejected under Section 112, second paragraph. Claims 60 and 76-81 are newly rejected under Section 102(b) as allegedly anticipated by McDonnell et al, Cell (1989) 57:79-88. Claim 75 is objected to under 37 CFR 1.75 as allegedly being a substantial duplicate of claim 70.

By this amendment, claims 72, 74, and 81 are amended, and claim 75 is canceled. Following entry of this amendment, claims 69-74, and 76-81 will be pending. No new matter is added by this amendment.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application.

***Specification and title***

The specification and title have been amended as requested by the Examiner. A copy of the ATCC deposit receipt is provided herewith to confirm that the bacterial strain referenced in page 16 of the specification was deposited with the American Type Culture Collection at Rockville, MD on February 7, 1994 and given Accession No. 69555.

[1] Applicants note that the Summary of the Office Action states that claims 69-81 are rejected. However, only claims 69, 70, 72, 74-81 are rejected in the body of the Office Action. Thus, claims 71 and 73 are not rejected, but are not indicted as allowed or allowable.

***Rejections under 35 U.S.C. § 112, second paragraph***

Claims 70, 72, 74, 80 and 81 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants respectfully traverse this rejection. Several grounds for rejection are provided, which are discussed in turn below.

Claim 70

Claim 70 is newly rejected as allegedly indefinite because "it is not clear that the nucleic acid sequence in claim 69 was introduced into the cell." The Examiner suggests that the phrase "wherein said nucleic acid is a viral vector" would overcome this rejection. Applicants respectfully traverse this rejection

Applicants respectfully submit that the present language is clear. Clarification is requested for the basis of the rejection, which is not understood. Applicants further note that the present claim language was introduced into the claim based on a suggestion made during the interview held April 9, 2003 with the Examiner, Examiner Reynolds, and SPE Elliott. Withdrawal of this rejection is respectfully requested.

Claim 72

Claim 72 is rejected as allegedly indefinite for recitation of claim 69 in the body of the claim. This rejection is traversed, as claim 70 has been amended to recite the phrase "wherein there are two or more copies of said nucleic acid sequence", as helpfully suggested by the Examiner. Withdrawal of this rejection is respectfully requested.

Claim 74

Claim 74 is newly rejected as allegedly indefinite because the phrase" the first framework region of said N-terminal variable region" lacks antecedent basis. By this amendment, the claim has been amended and now recites "a first framework region of said N-terminal variable region". Applicants believe that this amendment addresses the Examiner's concern that the phrase allegedly lacks proper antecedent basis. Withdrawal of this rejection is respectfully requested.

The Examiner further queries "what is a framework region". Office Action, page 4. To the extent that this is asserted as a basis for the indefiniteness rejection, Applicants respectfully note that the meaning of "framework region" is well known in the art: the framework regions are relatively invariant regions in the variable domains of immunoglobulins that provide a protein scaffold for the hypervariable regions. As is known in the art, there are four framework regions, which surround the three hypervariable regions (CDRs), and the most amino-terminal framework region is the "first framework region". Accordingly, Applicants submit that this language is clear. For the above-stated reasons, withdrawal of this rejection is respectfully requested.

Claim 80

Claim 80 is rejected as indefinite because the term "autoimmune antigen" is allegedly indefinite "for reasons of record regarding autoantigen." For the Examiner's convenience, Applicant will briefly summarize the grounds for rejection of the term "autoantigen" previously stated in the file of the present application:

(a) In the Office Action mailed December 19, 1999, the term "autoantigen" was rejected as allegedly indefinite because

> an antigen that is recognized as a "self antigen" in one person may not be recognized as "self antigen" in a different person. The term "autoantigen" is not defined in the specification and does not have an art recognized meaning; therefore; the term is indefinite.

(b) In the advisory action dated 5/20/00, the Examiner further stated:

> Applicants argue that the term "autoantigen" is defined as "self antigen" and any tissue constituent that evokes an immune response. Applicants argument is not persuasive. The term is confusing because applicants invention is attempting to prevent an immune response while the definition sates autoantigens evoke an immune response. The term is also relative because the immune system may recognize self-antigens during development to induce tolerance but eventually does not respond to self-antigens under normal conditions. In addition, the tem "autoantigen" is used in relation to a person which is not recited in the claim. For example, the melanoma antigen MART-1 is an autoantigen in every melanoma patient. Therefore, the metes and bounds of antigens which are "autoantigens" cannot be determined.

(c) in the Office Action mailed 12/20/02, the Examiner maintained the rejection stating

> the metes and bounds of proteins encompassed by the term "autoantigen" cannot be determined. Applicants argue that the term has an art recognized meaning which is "any tissue constituent that evokes an immune response to the host's tissue." Applicants argument is not persuasive. Proteins capable of evoking an immune response within a host include factor VIII, acetylcholine receptors, collagen, MBP, thyroglobulin and MHC molecules. However, the term :autoantigenic" also describes proteins relative to their host. Would factor VIII isolated from healthy individuals be included in the claim or would factor VIII have to be isolated from a person who had an autoimmune response against it? Thus, it is unclear if the term refers only to protein isolated from a host having an autoimmune response against that protein or if it can be isolated from a healthy individual.

Applicants respectfully traverse this rejection. Applicants have provided dictionary definitions of the term "autoantigen" that have been ignored by the Examiner. As previously stated in the response filed May 9, 2000:

> Applicants respectfully urge the Office to reconsider its determination that the recitation of the term "autoantigen" renders the claims unclear or indefinite (see: Official Action, page 6, last paragraph). While most mammalian subjects respond in varying degrees to different antigenic epitopes, autoantigen is, contrary to the Office's contention, an art recognized term and its use herein is consistent with such usage. For example, autoantigen is defined as: "[a] 'self' antigen; any tissue constituent that evokes an immune response to the host's tissues" (see: Stedman's Medical Dictionary, page 170, right column, fifth entry from bottom of page (26th Ed. Williams and Wilkins, Baltimore, MD)).

As further stated in the response filed May 21, 2003:

> [w]ith regard to the Examiner's allegation that the term "autoantigens" is not defined in the specification and does not have an art recognized meaning, Applicants respectfully submit that the term does in fact have a meaning that is well known in the art. For example, Stedman's Medical Dictionary (26th Edition) defines the term as "any tissue constituent that evokes an immune response to the host's tissues." As illustrated in Janeway et al., Immunobiology, pages 489-509, 4th ed., autoantigens are self-antigens associated with auto-immune diseases in which individuals develop autoantibodies to self-antigens.

> Illustrative examples of autoantigens are also provided in the specification, for example at page 10, lines 25-28.

Applicants respectfully submit that it has repeatedly been demonstrated to the Office that the term "autoantigen" is clear and that one of skill in the art understands the meaning of "autoantigen", as evidenced by several dictionary definitions that have been entered into the present record. Illustrative examples of autoantigens are also provided in the specification, e.g., at page 10, lines 25-28. Applicants submit that the equivalent term "autoimmune antigen" is similarly clear (see, e.g., definition of "autoantigen", above, which states that autoantigens are self-antigens associated with auto-immune diseases."). Withdrawal of this rejection is respectfully requested.

Claim 81

Claim 81 is rejected as allegedly indefinite for reciting "allergan". The Examiner states that the term "cannot be found in the art" and further that the term is not defined in the dictionary or specification.

The claim has been amended and now recites "allergen." Applicants apologize for the misspelling. Support for the amendment is found in the specification at, e.g., page 10, line 25. Applicants submit that the term is clear, and the meaning of the term is well-understood by one of skill in the art. Applicants note that claims using the term "allergen" have not previously been rejected as allegedly indefinite. Withdrawal of this rejection is respectfully requested.

***Rejection under 35 U.S.C. § 102***

Claims 69 and 76-81 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by McDonnell et al. (Cell, 1989, Vol. 57 pg 79-88) ("McDonnell"). Specifically, the Examiner cites McDonnell for teaching:

> a transgenic mouse whose genome comprises a transgene comprising bcl-2-Ig fusion protein. Splenocytes and thymocytes were isolated from the mice in saline and media. The splenocytes and thymocytes are non-tumor lymphoid cells and are equivalent to the composition claimed because they have the structure claimed. The bcl-2 fusion protein is equivalent to the fusion protein required in the claim

> because it has a heavy chain immunoglobulin and bcl-2. The cells of McDonnell inherently "induces tolerance to an antigen" because it has the same structure as the cell claimed. (Office Action, page 5).

The Examiner further states (Office Action, page 5) that:

- the phrase "for introduction into an individual" does not bear patentable weight;
- that splenocytes and thymocytes are "bone marrow cells" as required in claim 77 "because they originated in the bone marrow";
- that splenocytes and thymocytes inherently have "B-cell" as required by claim 78 "because B-cells are found in the spleen and thymus";
- that splenocytes and thymocytes inherently comprise "hematopoietic cells" as required by claim 81 "because they comprise pluripotent cells capable of differentiation"; and
- that claims 82 and 83 are included in the rejection "because the metes and bounds of the limitations cannot be determined (see 112/2d); therefore bcl-2 is an autoimmunogen and an allergen".

Applicants respectfully traverse this rejection because a prima facie case of anticipation has not been made for at least the following reasons:

- claims 76, 77, and 78 are improperly rejected, as the claims depend from claim 70, which has not been rejected as anticipated over McDonnell;
- the Examiner as provided no evidence that the minigene of McDonnell encodes a *fusion protein having a heavy chain immunoglobulin and bcl-2*, as stated by the Examiner in the Office Action;
- the Examiner has not demonstrated that McDonnell inherently discloses a pharmaceutical composition that "induces tolerance to the antigen in the individual" as required by the present claims;

- cells comprising McDonnell's minigene are not "cells suitable for introduction into an individual", as required by the present claims;
- the cells of McDonnell are not present in pharmaceutical compositions and do not comprise a pharmaceutically acceptable excipient as required by the claims
- splenocytes and thymocytes are not bone-marrow cells;
- splenocytes and thymocytes are not hematopoietic cells; and
- no evidence is provided that bcl-2 is an autoimmune antigen or an allergen.

Applicants will now discuss these points in greater detail.

(1) Claims 76, 77, and 78 are improperly rejected

Applicants respectfully submit that the rejection of claims 76, 77, and 78 is improper. These claims depend from claim 70, which is not rejected as allegedly anticipated by the McDonnell reference. Because claim 70 is not anticipated by McDonnell, claims 76, 77, and 78, which depend from claim 70, are also free of McDonnell. Accordingly, withdrawal of the rejection of claims 76, 77, and 78 is respectfully requested.

(2) the Examiner as provided no evidence that the minigene of McDonnell encodes a *fusion protein having a heavy chain immunoglobulin and bcl-2*

McDonnell is cited as disclosing "a transgenic mouse whose genome comprises a transgene comprising bcl-2-Ig fusion protein" and that "[t]he bcl-2 fusion protein is equivalent to the fusion protein required in the claim because it has a heavy chain immunoglobulin and bcl-2." *See* Office Action, page 5. Applicants respectfully traverse this rejection.

A prima facie case of anticipation has not been made, because McDonnell neither teaches nor suggests that a bcl-2-Ig fusion protein is expressed, contrary to the Examiner's statements in the Office Action. By contrast, McDonnell discloses a transgenic mouse harboring a bcl-2-Ig *fusion gene*, termed a mini-gene, encompassing human genomic DNA sequences found at the breakpoint of

the t(14:18) interchromosomal translocation.[2] *See* McDonnell at Figure 1 (showing the structure of the transgene), and at page 86, left column (describing preparation of the transgene). Although the minigene (transgene) is described as "cDNA" by McDonnell, the minigene actually encompasses part of the bcl-2 genomic region, joined to part of the bcl-2 cDNA, joined to genomic DNA making up part of the heavy chain immunoglobulin genomic locus (see McDonnell, page 86, left column, last paragraph). The effects of bcl-2 overexpression on B cell longevity and development are studied in transgenic mice that comprise the transgene. Tolerance induction is not disclosed in McDonnell, nor is any evidence of expression of a fusion protein comprising bcl-2 and immunoglobulin shown in McDonnell. McDonnell merely states that bcl-2 is overexpressed, and shows transcription of only the bcl-2-portion of the transgene. Protein expression from the heavy chain immunoglobulin portion of the transgene is not even mentioned, and, indeed, McDonnell does not even demonstrate that the immunoglobulin region of the transgene is transcribed.

Indeed, one of ordinary skill would not expect that McDonnell's transgene would encode a fusion protein comprising bcl-2 and heavy chain immunoglobulin for a number of reasons.

First, McDonnell's transgene consists of bcl-2 cDNA linked to genomic DNA sequences corresponding to part of the heavy chain genomic locus. McDonnell does not state that the immunoglobulin coding regions are in frame with bcl-2 coding regions, such that a fused bcl-2-Ig transcript would encode the immunoglobulin sequences in the proper frame. Proper translation of heavy chain immunoglobulin requires in-frame transcription, such that the immunoglobulin will be properly translated. Next, it is well known that heavy chain immunoglobulin protein expression requires genomic rearrangement within the heavy chain locus and proper mRNA splicing. By contrast, the Examiner has provided no evidence that the transgene immunoglobulin sequences would be properly rearranged and/or spliced, such that immunoglobulin sequences are properly translated. Applicants note in this regard that the t(14:18) translocation mimicked in the transgene is believed to arise during aberrant immunoglobulin gene rearrangement. Finally, heavy chain

[2] The t(14:18) translocation is a human chromosomal translocation found in 85% of follicular small celled B cell lymphomas, and is believed to arise during attempted Ig gene rearrangement, introducing the bcl-2 gene from chromosomal location 18q21 into the Ig heavy chain locus at 14q32. See McDonnell, page 79, right column.

regulatory elements and introns are missing from the fusion gene, as the transgene lacks portions of the immunoglobulin genomic locus. Proper translation and/or splicing of heavy chain may require presence of regulatory elements or introns that are absent from the transgene.

Accordingly, it is evident that one of skill in the art would not expect that the transgene would encode a fusion protein comprising both bcl-2 *and* immunoglobulin polypeptide sequences as required by the present claims. Thus, the Examiner has not made a prima facie case of anticipation, because the Examiner has not demonstrated that each and every element of the claim is disclosed by the cited reference. Withdrawal of this rejection is respectfully requested.

(3) The Examiner has not demonstrated that McDonnell inherently discloses a pharmaceutical composition that "induces tolerance to the antigen in the individual"

In the Office Action, the Examiner further states that

> [t]he composition of McDonnell inherently meets the functional limitation of "wherein upon introduction [in]to an individual said composition induces tolerance to the antigen in the individual" because it has the structure claimed. (Office Action, page 5).

The examiner has not made a prima facie case that McDonnell inherently discloses the pharmaceutical compositions of the present claims. The requirements for a rejection based on inherency are stated in M.P.E.P. § 2112, which describes the Examiner's burden in making such a rejection:

> In relying on the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. (M.P.E.P. § 2112 (emphasis in original)).

Moreover, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." Id. (quoting In re Oelrich, 212 USPQ 323, 326 (CCPA 1981).[3]

[3] The M.P.E.P. is in accordance with well-established case law addressing inherency. To serve as an anticipation when the reference is silent about the asserted inherent characteristic, the missing descriptive matter must be shown to be necessarily present in the thing described in the reference, and that it would be so recognized by the person of ordinary skill in the art. See Continental Can Co. v. Monsanto Co., 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). "Inherency may not be established by probabilities or possibilities," In re Oelrich, 212 USPQ 323, 326 (CCPA 1981), and "occasional results are not inherent." Mehl-Biophile Int'l Corp. v. Milgraum, 52 USPQ2d 1303, 1306 (Fed. Cir. 1999).

Accordingly, in order to make a prima facie case of inherent anticipation based on the cited reference, the Examiner is required to advance a basis in fact and/or technical reasoning to reasonably support the assertion that administration of the cells disclosed in McDonnell necessarily results in tolerance upon introduction to an individual as required by the present claims.

This the Examiner has not done. Instead, the Examiner merely states that "[t]he composition of McDonnell inherently meets the functional limitation of 'wherein upon introduction [in]to an individual said composition induces tolerance to the antigen in the individual' because it has the structure claimed". However, as noted above, McDonnell does not disclose a fusion protein, and the Examiner has provided no evidence that expression of the fusion *gene* of McDonnell encodes a fusion *protein* as required by the claims. Accordingly, Applicants respectfully submit that the Examiner has not demonstrated that the composition of McDonnell "has the structure claimed", and thus, the Examiner cannot rely upon this assertion as a basis for the inherency rejection.

No additional evidence or technical reasoning is provided by the Examiner that demonstrates that administration of the cells of McDonnell necessarily results in tolerance when introduced into an individual. Indeed, as noted above, Applicants submit that one of ordinary skill would not necessarily expect that McDonnell's transgene would encode a fusion protein comprising bcl-2 and heavy chain immunoglobulin.

Accordingly, a prima facie case of inherent anticipation has not been made, and withdrawal of this rejection is respectfully requested.

(4) Cells comprising McDonnell's minigene are not "cells suitable for introduction into an individual", as required by the present claims.

As a preliminary matter, Applicants disagree with the Examiner's assertion that

> [t]he phrase "for introduction into an individual" does not bear patentable weight because they are intended uses and may not occur. These intended uses do not bear patentable weight because they do not alter the structure of the compositions. (Office Action, page 5).

The Examiner has mischaracterized the language of claim 69 in the rejection. Applicants note that the claim recites "a non-tumor lymphoid cell or non-tumor hematopoietic cell *suitable* for introduction into an individual" (not just "for introduction into an individual", as quoted by the

Examiner). Review of the claim indicates that this phrase bears patentable weight, because the claim affirmatively requires use of a cell *suitable* for introduction into an individual. Accordingly, it is evident that the quoted language does bear on the "structure" of the composition, to use the Examiner's words.

Turning to the substance of the McDonnell reference, Applicants submit that the cells of McDonnell are not "cells that are suitable for introduction into an individual", for the purpose of tolerance induction, as required by the present claims. McDonnell's cells comprising the bcl-2-Ig minigene overexpress the bcl-2 gene, a phenotype that is characterized as "a primary mechanism of neoplasia" by McDonnell (see, page 84, right column). Overexpression of the bcl-2 gene from the transgene resulted in immortalization of a subset of splenocytes predominantly of mature B cell phenotype, which is described as "a pathological consequence" and "reminiscent of the disease from which bcl-2 was isolated" (i.e., B cell lymphoma, a cancer characterized by uncontrolled expansion of malignant B cells). Applicants respectfully submit that immortalized cells that overexpress the bcl-2 gene, a gene implicated in neoplasia and B cell lymphoma, such that the cells are immortalized and reminiscent of a cancer phenotype are not "cells suitable for introduction into an individual", particularly in view of the purpose of the present claim, tolerance induction. Withdrawal of this rejection is respectfully requested.

(5) the cells of McDonnell are not present in pharmaceutical compositions and do not comprise a pharmaceutically acceptable excipient as required by the claims.

In the Office Action, the Examiner states "[s]plenocytes and thymocytes were isolated from the mice in saline and media and are equivalent to the composition claimed because they have the structure claimed." (Office Action, page 5). Thus, the Examiner appears to take the position that McDonnell discloses pharmaceutical compositions comprising a pharmaceutically acceptable excipient. Applicant believes that the Examiner is referring to the following excerpt from McDonnell in support of this proposition (the Examiner did not provide a page citation in the Office Action):

> Single-cell suspensions were prepared from 8- to 9-week-old mice by mincing whole spleen or thymus and then pressing fragments between sterile frosted glass slides in Hanks' balanced salt solution. Organ capsules and connective tissue remnants were discarded. Cells were

> sedimented at 100 x g for 10 min, then resuspended in DMEM supplemented with 5% fetal calf serum and 100U/ml penicillin-streptomycin. (McDonnell, page 86, right column)

Review of this excerpt indicates that whole spleen and thymus, or minced whole spleen and thymus absent organ capsules and connective tissue were suspended in HBSS. Applicants disagree that this mixture comprises a pharmaceutical composition. One of skill in the art would not believe that HBSS comprising minced whole organ (even lacking the capsid and connective tissue) constituted a pharmaceutical composition.

Further review of this excerpt indicates that single cell suspensions were prepared in DMEM tissue culture media in the presence of 5% fetal calf serum and 100U/ml penicillin-streptomycin. Applicants vigorously disagree that tissue culture media including fetal calf serum and antibiotic constitutes a pharmaceutically acceptable excipient, as required by the present claims.

The McDonnell reference also discloses the incubation of single cell suspensions in the presence of primary rat anti-mouse monoclonal antibodies, and fluorescence-coupled secondary antibody, then resuspension of now-fluorescently labeled cells in PBS containing 0.1% bovine serum albumin and 2 ug/ml propidium iodide (McDonnell, page 86, right column). Applicant also disagree that these suspensions, which include rat anti-mouse antibodies and labeled secondary antibodies, and/or propidium iodide and BSA, comprise pharmaceutical composition or encompass a pharmaceutically acceptable excipient. Withdrawal of this rejection is respectfully requested.

(6) Splenocytes and thymocytes are not bone-marrow cells.

Regarding claim 77, as noted above, Applicants submit that this claim is improperly rejected as this claim depends from claim 70, which is not rejected as allegedly anticipated by McDonnell. In addition, the Examiner states that splenocytes and thymocytes are bone marrow cells. Applicants disagree with the Examiner's assertion that splenocytes and thymocytes are "bone marrow cells because they originated in the bone marrow". Splenocytes are spleen cells, and thymocytes are cells of the thymus. Splenocytes and thymocytes are not bone marrow cells. Withdrawal of this rejection is respectfully requested.

(7) Splenocytes and thymocytes are not hematopoietic cells.

The Examiner rejected claim 81 on the ground that splenocytes and thymocytes "inherently comprise hematopoietic cells . . . because they comprise pluripotent cells capable of differentiation". Claim 81 does not recite "hematopoietic cells". Accordingly, the rejection of claim 81 is improper and should be withdrawn.

Applicants will now address this rejection to the extent that it may be deemed to apply to claim 79, which recites "hematopoietic cells." Applicants respectfully traverse this rejection. Applicants submit that the Examiner's definition of hematopoietic cells as "pluripotent cells capable of differentiation" is overbroad and incorrect. As defined in the specification:

> [a] "hematopoietic cell" is a cell that can form blood cells include[sic: including] lymphocytes and macrophages from such tissues [such] as bone marrow cells and other extramedullary tissues (specification, page 7, lines 14-16).

Applicants disagree that splenocytes and thymocytes are hematopoietic cells, as the term is defined in the specification, and the Examiner has provided no evidence that hematopoietic cells are found in the spleen or thymus. Accordingly, withdrawal of this rejection is respectfully requested.

***Double Patenting***

Claim 75 is objected to under 37 CFR 1.75 as allegedly being a substantial duplicate of claim 70. To expedite prosecution and without conceding the propriety of this rejection, claim 75 is cancelled. Withdrawal of this rejection is respectfully respected.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

In the unlikely event that the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 308072000110. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 24, 2003

Respectfully submitted,

By Cara Coburn

Cara M. Coburn
Registration No.: 46,631
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304
(650) 813-4218

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PATENT & TRADEMARK OFFICE

American Type Culture Collection
12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

*INTERNATIONAL FORM*

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

**To: (Name and Address of Depositor or Attorney)**

David W. Scott, Ph.D.
University of Rochester
601 Elmwood Ave., Box 704
Rochester, NY 14642

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**Deposited on Behalf of:** David W. Scott, Ph.D.

| **Identification Reference by Depositor:** | **ATCC Designation** |
|---|---|
| Escherichia coli DH5α, pQ3.EZ | 69555 |

The deposit was accompanied by: __ a scientific description X a proposed taxonomic description indicated above.

The deposit was received February 8, 1994 by this International Depository Authority and has been accepted.

**AT YOUR REQUEST:**

X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested February 14, 1994. On that date, the culture was viable.

**International Depository Authority:** American Type Culture Collection, Rockville, Md. 20852 USA

**Signature of person having authority to represent ATCC:**

Bobbie A. Brandon  **Date:** February 14, 1994

**Bobbie A. Brandon, Head, ATCC Patent Depository**

cc: Kathy Kowalchyk

**Form BP4/9**